



FLORIDA  
INTERNATIONAL  
UNIVERSITY

# MICE

## Biology & Husbandry

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# Taxonomy

Mus Musculus

The house mouse of North America and Europe is the most frequently used animal in biomedical research.

Kingdom: Animalia

Phylum: Chordata

Class: Mammalia

Order: Rodentia

Suborder: Myomorpha

Family: Muridae

Genus: Mus

Species: musculus



# Taxonomy

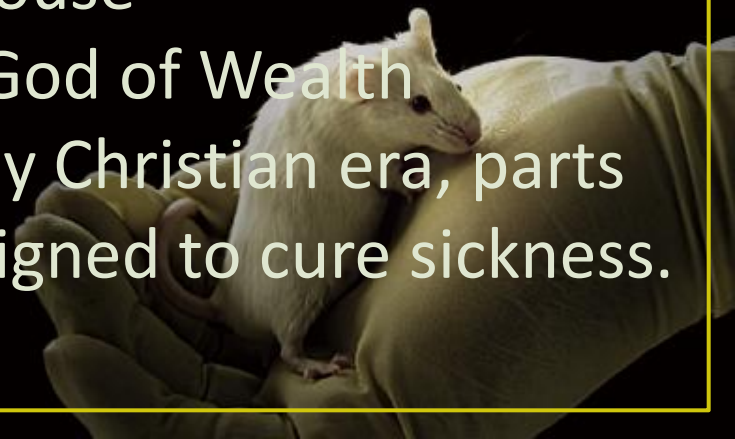
- European Mouse
  - *Mus musculus musculus* (eastern)
  - *Mus musculus domesticus* (western)
- Western European Mouse (Mediterranean)
  - *M. spretus*
- Asian mice
  - *Mus musculus castaneus* (Thailand)
  - *Mus musculus molossinus* (Japan)



# History

In some cultures, mice were protected and worshipped.

1. The Greeks built a temple to Apollo Smintheus, the Mouse God, in gratitude for mice supposedly chewing the leather of their adversaries shield in 1500 BC.
2. Chinese and Japanese have a long relation with the mouse.
  - Every 12 years=Year of the Mouse
  - 11AM-1Pm=Hour of the Mouse
  - Mouse=Messenger of the God of Wealth
3. During late Greco-Roman and early Christian era, parts of mice were included in potions designed to cure sickness.



# History

- Clarence C. Little in 1909 was investigating coat colors of mice and had began inbreeding mice with coat colors of dilute (d), brown (b), and non-agouti (a). His dba strain became the DBA strain still popular today. He also developed C57BL/10, C57BR, C57BL/6, and C57L.
- Dr. Little established Jackson Labs in 1929 and was a recipient of The Nobel Prize.
- Leonell C. Strong (1919), a cancer geneticist, was the originator of the inbred strains A, C, CBA, C3H, BRSUNT, CHI, F, I, JK, H, NH, STR, BDP, and SEC.
- In 1926, Clara Lynch imported several pairs of mice from Lausanne, Switzerland - the progenitors of the major inbred and outbred “Swiss”.



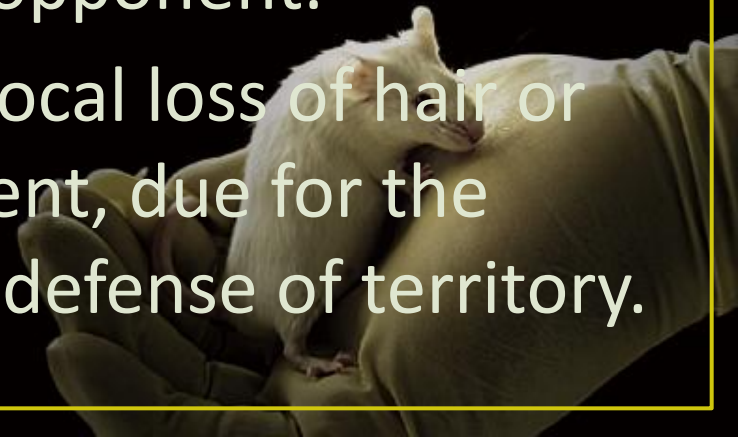
# Strain Abbreviations

Strain	Abbreviation
AKR	AK
BALB/c	C
C3H	C3
RIII	R3
DBA/1	D1
DBA/2	D2
C57BL	B
C57BL/6	B6
C57BL/10	B10
C57BR	BR
C57L	L



# Description

- Present many similarities with rats. Separated from them over 24 Million years.
- Generally not terribly aggressive, will rather evade than confront.
- Can live up to 3 years.
- Males housed together will probably fight sometimes to the death of the opponent.
- The phenomena of barbering (focal loss of hair or whiskers with no wounds) present, due for the establishment of hierarchy and defense of territory.



# Anatomy & Physiology

## External Features

1. Long tail
2. Erect rounded ears
3. Bright eyes
4. Pointed snout with vibrissae



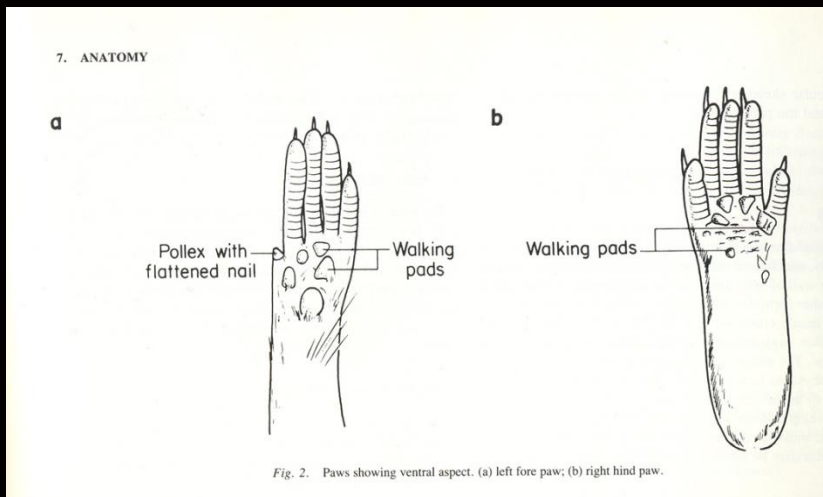


# Anatomy & Physiology

## External Features

5. Short legs, feet with 5 toes on each foot.

The first digit on the front feet (pollex) lacks a middle phalanx and is very small. The feet have walking pads and rudimentary sweat glands open to the surface of the foot pads.

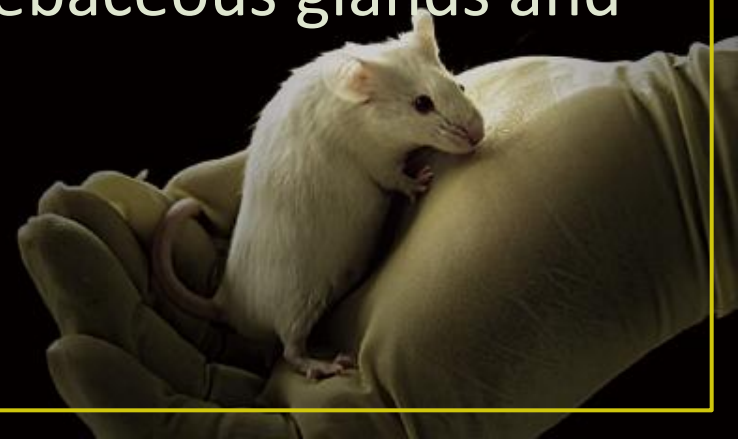


# Anatomy & Physiology

The mouse has no hair on the nose, palms, lips and soles.

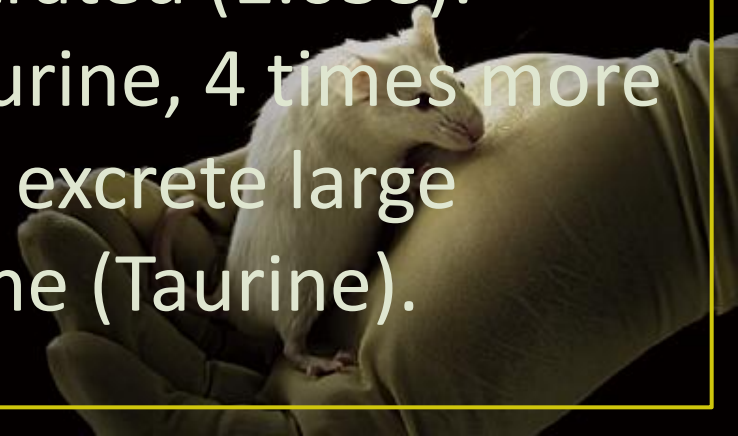
The mouse hair coat is composed of two classes of hairs tactile and pelage.

- Tactile hairs have associated venous sinuses, glands, and nerve endings. They are larger and longer than pelage hairs.
- Pelage hairs are associated with sebaceous glands and smooth muscle (erector pili).



# Anatomy & Physiology

- Thermoregulation: Mice are poor regulators of body heat and can die at 99°F.
- Normal rectal temperature is 95-102.5°F.
- Cardiovascular:
  - HR = 320-840/min; BP = 120/80 mm Hg
- Respirations: 84-280 breaths /min
- Renal: Urine is highly concentrated (1.058). Males have strongly scented urine, 4 times more allergenic than females. Mice excrete large amounts of protein in the urine (Taurine).



# Anatomy & Physiology

Dental Formula

I 1/1, C 0/0, PM 0/0, M 3/3) x 2 = 16

Incisors grow continuously.

Can result in overgrowth and resulting malocclusion.

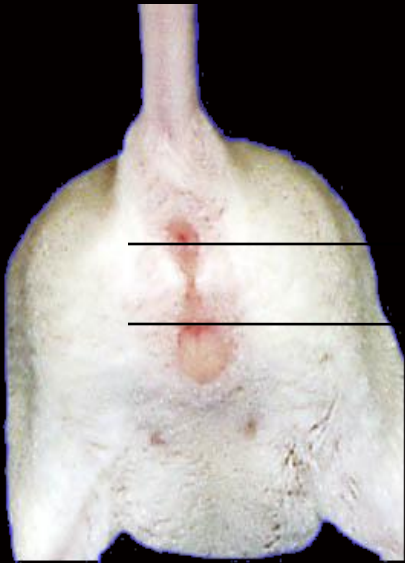


# Anatomy & Physiology - Males

- Os penis
- Open inguinal ring

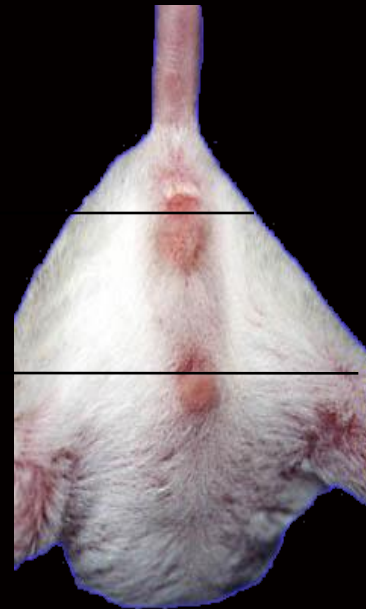


# Sexing - Anogenital distance



Female

Anogenital distance is 1.5-2 times greater in the male than in the female.



Male

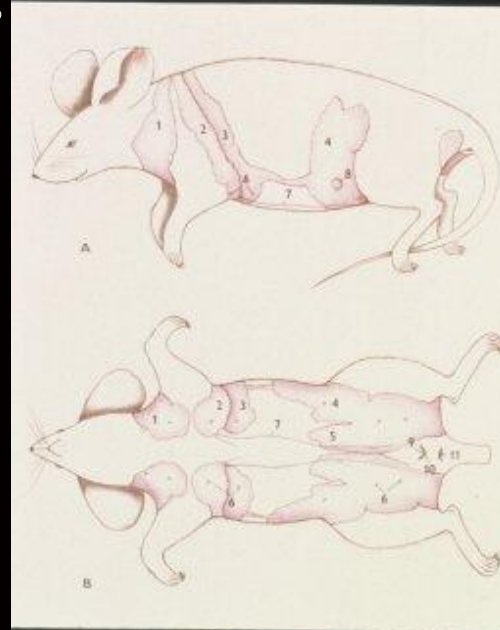


# Anatomy & Physiology - Female

Five pairs of nipples and mammary glands

- 3 thoracic
- 2 inguinal

The male has no nipples.



# Anatomy & Physiology - Female

Effect of pheromones on reproduction - Lee-Boot effect

- When female mice are housed together in small groups (4-5) without a male present, there is an increase in the incidence of spontaneous pseudopregnancy.
- Overcrowded females (30-40/cage) tend to become anestrus. The effect is initiated by female odors. Its effect can be negated by excision of the olfactory nerve or by housing individually.

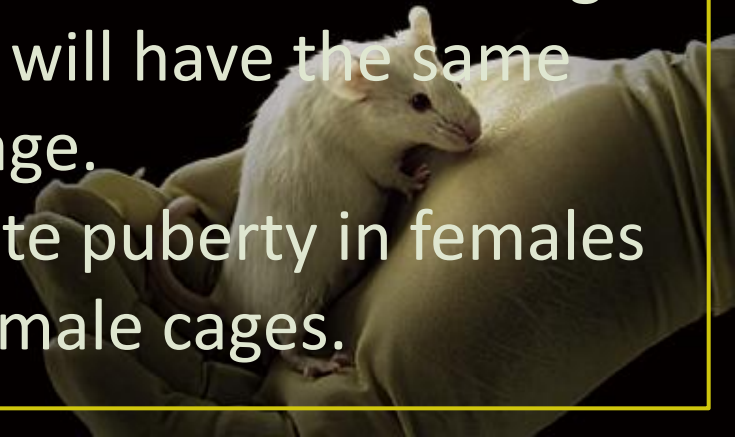




# Anatomy & Physiology - Female

Effect of pheromones on reproduction - Whitten effect

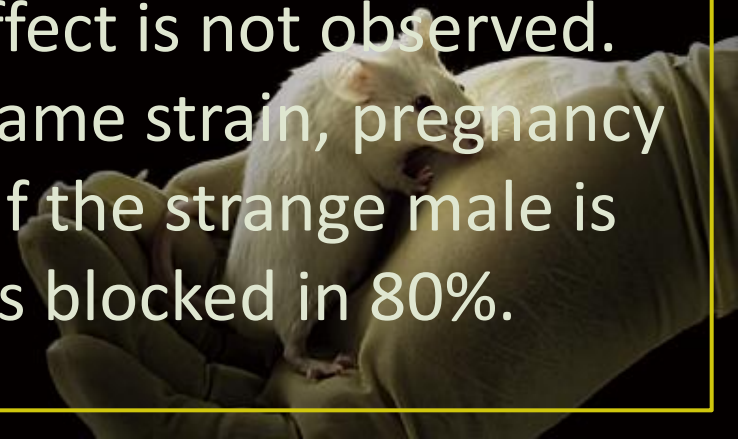
- If anestrus or pseudopregnant female mice are paired with a male, one half of the pairs will mate on the third night.
- Over 90% of the above pairs will mate within 5 days.
- Phenomenon described by Whitten as a post pairing synchrony of estrus. It is induced by a volatile substance in male urine. Placing the male next to the female cage (or placing male urine in the cage) will have the same effect as placing the male in the cage.
- The male pheromone will accelerate puberty in females that are exposed to bedding from male cages.



# Anatomy & Physiology - Female

Effect of pheromones on reproduction - Bruce effect

- If pregnant mice are exposed to a strange male during the preimplantation period (day 1-5 post breeding) the original pregnancy will be blocked/aborted. The effect is seen most frequently within the 24-48 hr post breeding period. Effect is mediated by an androgen-dependent olfactory pheromone contained in male urine. If the olfactory nerve is cut, the Bruce effect is not observed.
- If the strange male was from the same strain, pregnancy is blocked in 30% of the females. If the strange male is from a different strain pregnancy is blocked in 80%.



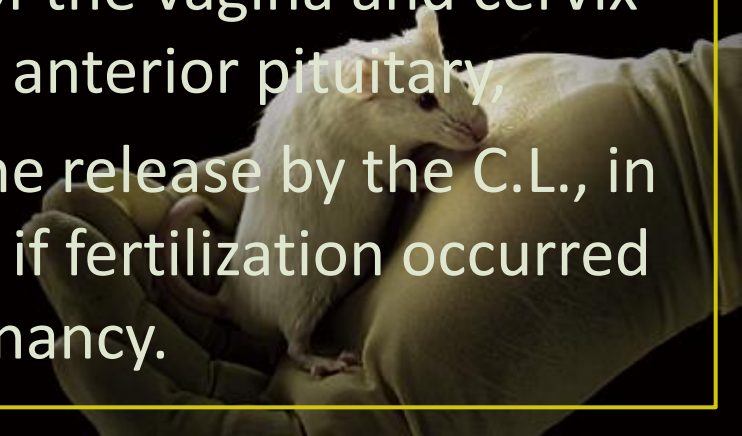
# Anatomy & Physiology

- Reproduction
  - Puberty occurs between 28-49 days of age (35 average)
  - Polyestrous all year round, spontaneous ovulators. Estrous cycle; 4-5 days.
  - Vaginal plug formed at copulation contains a mixture of vesicular and coagulating gland secretions. Vaginal plug usually fills the vagina from the cervical canal to the vulva. Vaginal plug usually persists for 18-24 hrs. 80-90% of mice with vaginal plugs become pregnant.



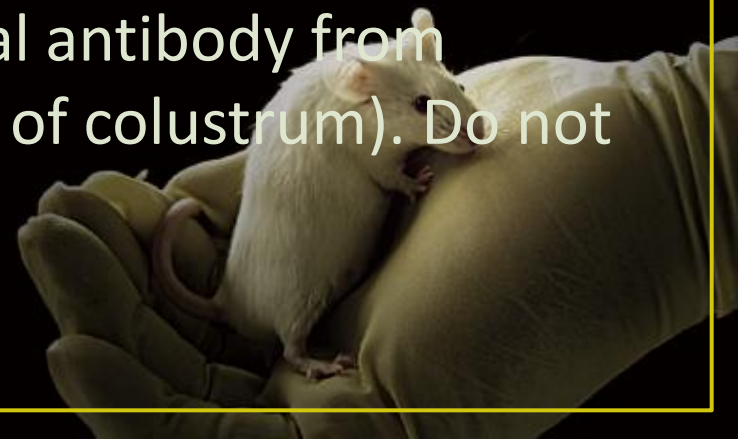
# Anatomy & Physiology

- Reproduction
  - Postpartum estrus – 20 to 24 hr after parturition. If the female is bred during postpartum estrus there can be a period of delayed implantation which last 4-10 days. Gestation will be extended the same amount of time.
  - Post lactation estrus – 2 to 4 days after removal of the litter.
  - Pseudopregnancy: Stimulation of the vagina and cervix leads to prolactin release by the anterior pituitary
  - Prolactin stimulates progesterone release by the C.L., in 13 days, the placenta takes over if fertilization occurred - otherwise termed pseudopregnancy.



# Anatomy & Physiology

- Gestation – 19 to 21 days.
- When mice are born they are:
  - Altricial - hairless and blind,
  - Nidicolous – helpless,
  - Bald- fully haired by 14 days of age.
  - Require milk - weaned at 21 days of age. Eat solid food at 11 days.
  - Lack immunity - require maternal antibody from colostrum (intestinal absorption of colostrum). Do not receive antibody in utero.
- Lack teeth.



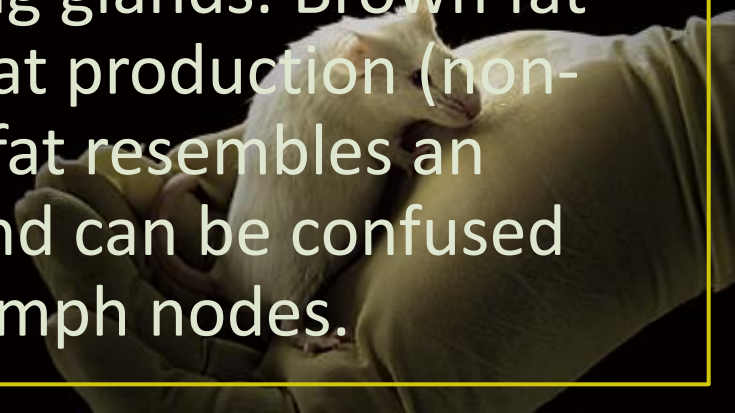
# Anatomy & Physiology

- Hearing:
  - Highly developed hearing
  - Born deaf, but can hear by 21 days.
- Repeated exposure to high pitch sound can cause growth retardation and influence reproduction. DBA/2 mice are susceptible to audiogenic seizures.
- Vision:
  - Eyes open at 14 days, Poor sight
  - Retina is composed almost entirely of rods (lack cones = poor color vision)



# Anatomy & Physiology

- Lungs - single lobe on left, 4 lobes on right.
- Esophagus; covered by striated muscle throughout its length.
- Heart with ectopic calcification is also present in old mice.
- Brown fat; adjacent to the thymus, in the axillae, along the jugular veins, near the hilus of the kidney, and beside the urethra. The most prominent masses occur between the scapulae = hibernating glands. Brown fat can be metabolized to increase heat production (non-shivering thermogenesis). Brown fat resembles an endocrine gland microscopically and can be confused with salivary glands and cervical lymph nodes.



# Anatomy & Physiology

- Liver weighs more in female than male.
- Spleen of male mice may be up to 50% larger than that of female mice.
- Pancreas is a diffuse structure stretching over a portion of the small intestine.
- The right kidney is usually larger and located further anterior than the left. The male usually has larger kidneys than the female (male kidney heavier).





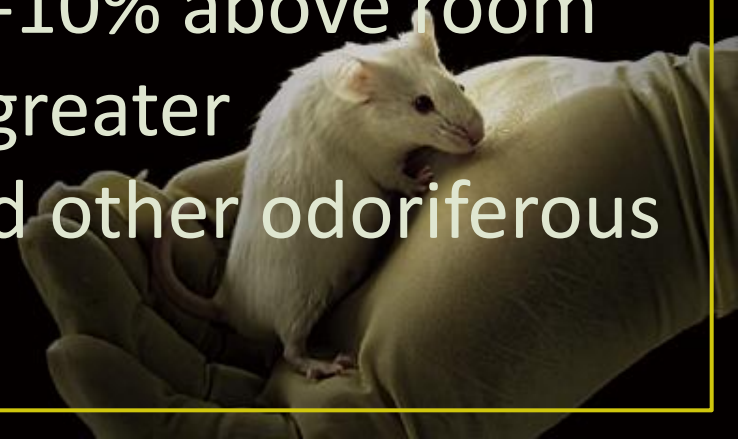
# Anatomy & Physiology

- Adrenals of female mice are consistently larger than those of males.
- Females that develop in utero between males may be masculinized (i.e. increased anogenital distance, male behavior, etc).
- Fecundity lower in winter, more males than females in summer.



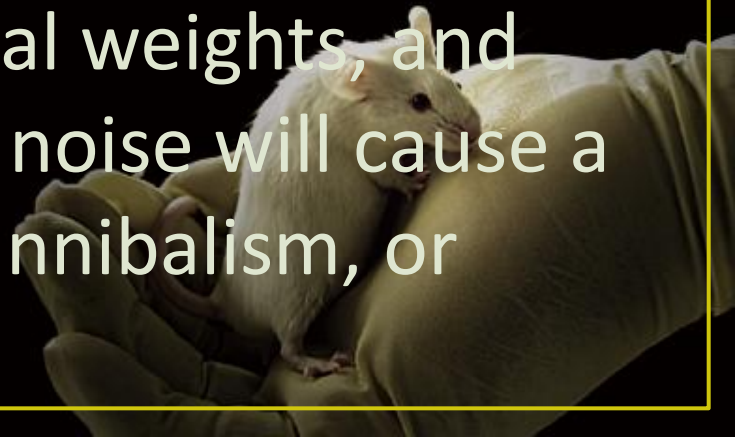
# Husbandry - Environment

- Room temperature is 68-79°F.
- Humidity is 30-70%.
- Air flow sufficient enough to provide for the heat load released from the primary enclosure.
- The environment within a mouse cage is higher in general, 1-4°F and R.H. of 5-10% above room environment, and will have a greater concentration of ammonia and other odoriferous substances.



# Husbandry - Environment

- Lights on automatic timer for 12-12 cycle. 30 foot candles at the working level (1 meter above floor).
- Noise must be controlled to a low level within housing area. Continuous levels above 85 dB can have auditory and non-auditory effects (eosinopenia, increased adrenal weights, and decreased fertility). Excessive noise will cause a sharp drop in reproduction, cannibalism, or audiogenic seizures.



# Husbandry - Caging

- Cages

(listed in order of decreasing cost and durability)

- Polysulfone
- Polyetherimide (PEI)
- Polycarbonate
- Polypropylene
- Polystyrene



# Husbandry - Caging

- Size Requirements

Weight	Floor area/animal	Height
<10 g	39 cm <sup>2</sup> (6 in <sup>2</sup> )	12.7 cm (5 in)
10-15 g	52 cm <sup>2</sup> (8in <sup>2</sup> )	“
16-25 g	77cm <sup>2</sup> (12in <sup>2</sup> )	“
>25g	97cm <sup>2</sup> (15 in <sup>2</sup> )	“
Female + Litter	330 cm <sup>2</sup> (51 in <sup>2</sup> )	“



# Husbandry - Bedding

- Bedding provides nesting material, absorbs feces and urine, and provides insulation. Bedding should be absorbent, not readily eaten, pathogen-free, non-injurious, and comfortable.
- Examples: hardwood chips, softwood chips, shredded paper and corncob bedding.
- It is important to note that bedding can influence experimental data and the type of bedding used should be described when the results of a study are published.



Soft Wood



Shredded Paper



# Husbandry - Bedding

- Corncob - inhibits hepatic microsomal enzymes, decreases reproductive efficiency, results in decreased ammonia formation in cages.
- Cellulose - decreases reproductive efficiency. Results in decreased ammonia formation in cages.
- Soft wood shavings - decreases barbiturate sleep time though stimulation of hepatic microsomal enzymes.
- Cedar - lower seizure threshold, induces hepatic microsomal enzymes.



# Husbandry - Water

- Water is usually offered free choice (ad libetum).
- Mice require 1.5 ml/10 g of BW/day, and drink about 6-7 ml of water/day.
- Water can be:
  - distilled,
  - from the tap,
  - from a reverse osmosis unit,
  - autoclaved,
  - Chlorinated (10-15 ppm)
  - Acidified (HCL @ pH 2.5-2.8)





# Husbandry - Water

- Water bottles or lixits are often used to deliver water to mice.
- When transporting mice gel packs, potatoes, sterilized canned food, or disposable pouches with a drinking valve can be used.



# Husbandry - Food

Feed formulation can be:

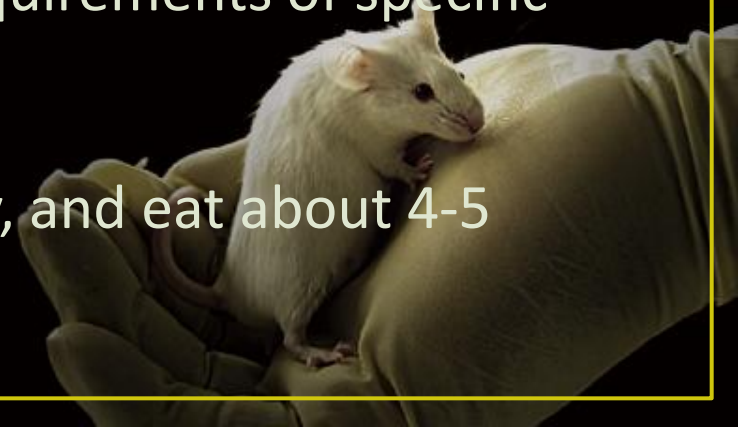
- Natural ingredient - diets formulated with processed whole grains and subjected to limited refinement. wheat, corn, oats, soybean meal, etc.
- Semipurified - only refined ingredients are used (i.e. casein, soy protein).
- Chemically defined - only chemically pure compounds (i.e. amino acids, vitamins, EFAs) are used. formulated with a combination of natural ingredients, pure chemicals and ingredients of varying degrees of refinement.
- Certified - diet which is guaranteed to have no more than a minimum level of chemohazards (i.e. estrogens, aflatoxins, heavy metals). Used in GLP studies.



# Husbandry - Food

Feed formulation can be:

- Closed Formula Diets- are commercial diets, where the ingredient composition is not readily available. The feed formula is the property of the manufacturer marketing the diet under a trade name.
- Open Formula Diets- are diets where the quantitative and qualitative ingredient composition is readily available. The formula can be adjusted to meet the requirements of specific research projects.
- Mice require 12 g of food/100 g BW/day, and eat about 4-5 g/day.



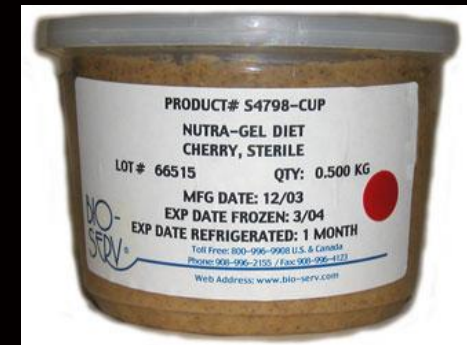
# Husbandry - Food

Feed Forms include:

- Pellets
- Semi moist
- Gel
- Liquid
- Powder

Feed treatment include:

- Autoclaving alters nutrient availability and may result in antimetabolites. Vitamin A, E, thiamin, riboflavin, and pantothenic (constituent of coenzyme A) acid may be lost.
- Pasteurization is done at 60°C for 30 minutes
- Irradiation is done at 4-5 mRads.



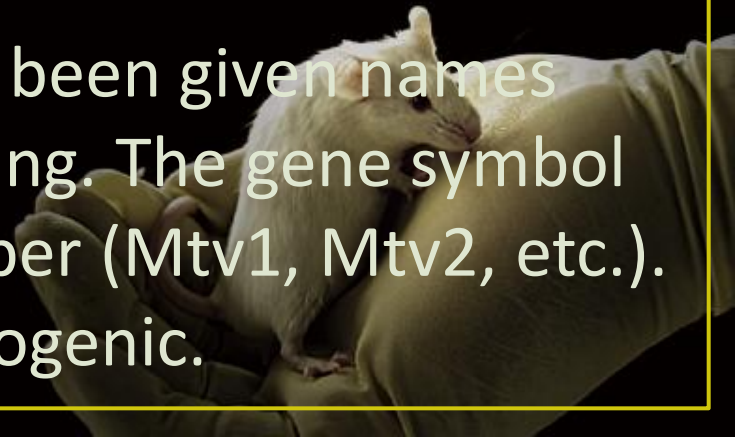
# Husbandry - Food

- Use food within 6 month of manufacture (mill) date (180 days for most diets; 90 days for diets with Vitamin C for NHP & G.Pig).
- Most chemically defined diets have a shorter shelf life.
- Store food at less than 70°F (22°C), and R.H. of ~ 50% or 4°C (fridge) for purified chemically defined diets.



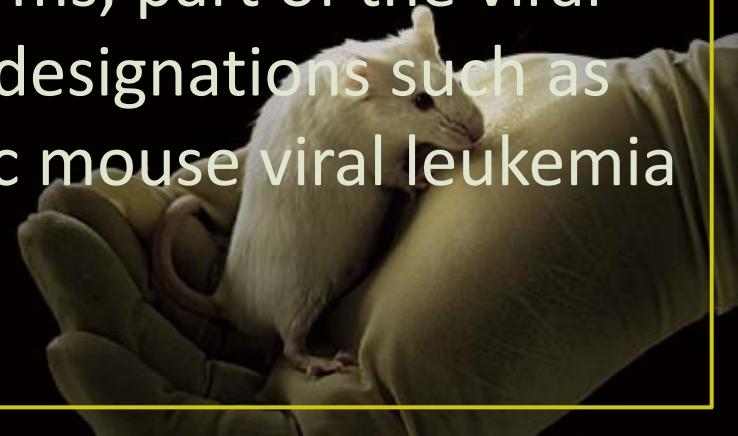
# Viral Infections

- Laboratory mice are host to a large spectrum of viral agents. Many have been eliminated from contemporary mouse colonies with modern husbandry practices.
- Murine retroviruses have not been eliminated. They exist in either an endogenous or exogenous form.
- Endogenous viruses, sometimes called “proviruses”, consist of viral DNA that has been integrated into the genomes of all strains of mice.
- These so called “proviruses” have been given names and included in genomic sequencing. The gene symbol Mtv is followed by the locus number (Mtv1, Mtv2, etc.). This form of the virus is lowly oncogenic.



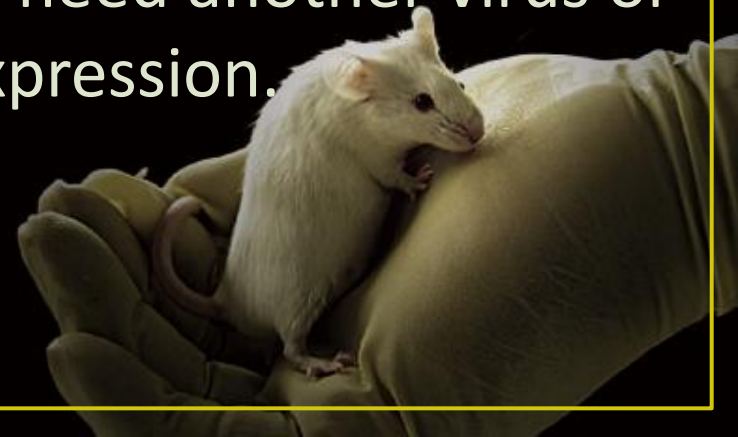
# Viral Infections

- The primary oncogenic virus that contributes to the development of mammary tumors in mice is MMTV-S, known as the Bittner virus. The virus is transmitted vertically through the milk of nursing dams but can also be transmitted through saliva and semen.
- Mouse Leukemia viruses are similar to Mammary Tumor Viruses regarding the presence of both endogenous and exogenous forms. Endogenous forms, part of the viral genome, are similarly given gene designations such as Emv1-1, which stands for Ecotropic mouse viral leukemia on chromosome #1.



# Viral Infections

- Mouse Leukemia Virus Clasification
  - Ecotropic strains are infectious to mouse cells in vitro.
  - Polytropic strains are infectious to both mouse and non-mouse cells in vitro
  - Xenotropic, to non-mouse cells only.
  - Some strains can also be considered incomplete or defective, which means they need another virus or inducer genes in order for expression.





# Virus Attributions

Virus	Family	Zoonotic	DNA	RNA	Enveloped	Non-enveloped	Host
Ectromelia	Poxviridae		X		X		Mice
MCMV	Herpesviridae		X				Mice
MTV	Herpesviridae		X				
MVM	Parvoviridae		X			X	Mice
MPV	Parvoviridae		X			X	Mice
MAd-1	Adenoviridae		X			X	Mice, Rats
MAd-2	Adenoviridae		X			X	Mice, Rats
Polyomavirus	Papovaviridae		X				
K Virus	Papovaviridae		X				
LDEV	Togaviridae			X			
LCMV	Arenaviridae	X		X	X		Mice, Hamsters, G. pigs, NHPs
Sendai	Paramyxoviridae			X	X		Mice, Rats, Hamsters, G. pigs, Rabbits
PV	Paramyxoviridae			X	X		Mice, Rats, Hamsters, G.pigs, Rabbits
Reo 1, 2, 3	Reoviridae			X	X		Mice, Rats, Hamsters, G.pigs
EDIM	Reoviridae			X		X	Mice
MHV	Coronaviridae			X	X		Mice
TMEV	Picornoviridae			X			
MMTV	Retroviridae			X			
MuLV	Retroviridae			X			
Hantavirus	Bunyaviridae	X		X	X		

